REMARKS

After entry of this amendment, claims 1-23 are pending. The claims have been amended without prejudice or disclaimer and find support *inter alia* in the original claims. Claim 2 finds further support in the specification, for example, at page 24, lines 14-28. Claim 3 finds further support in the specification, for example, at page 27, lines 44-45. Claim 17 finds further support, for example, in the original claims 13 and 16. No new matter has been added.

Sequence Listing

The Examiner objects to the Sequence Listing for failing to comply with the requirements of 37 CFR §§ 1.821-1.825. In response, Applicants submit herewith a revised Sequence Listing which conforms to 37 CFR §§ 1.821-1.825 *via* EFS-Web, and a Statement to Support Filing and Submission in Accordance with 37 CFR §§ 1.821-1.825. Amendments to the Sequence Listing find support in the original Sequence Listing and in the specification at page 24, lines 14-28 and page 49, lines 15-20. Furthermore, a paragraph directed to the incorporation of the Sequence Listing in the specification has been added. No new matter has been added to the Sequence Listing or the specification. Entry of this Sequence Listing into the application is requested.

Specification

The Examiner objects to the specification for missing headings and a brief description of the drawings. Applicants respectfully disagree. Applicants note that the headings recommended by the guidelines regarding the arrangement of the specification were inserted in the Preliminary Amendment dated January 24, 2005. However, to better comply with the guidelines, the specification has been further amended to insert the suggested headings in the more appropriate locations of the specification. Further, a section entitled "Brief Description of the Drawings" has been added at page 3. Support for the added brief description of the drawings is found in the specification at page 61, lines 29-30. No new matter has been added.

The Examiner further objects to the specification for referring to the only drawing provided at pages 66 and 68 of the specification as "fig. 4." In response, pages 66 and 68 of the specification have been amended to refer to the drawing as "fig. 1." No new matter has been added.

In view of the present amendments, it is believed that the above objections are overcome. Accordingly, reconsideration and withdrawal of the objections is respectfully requested.

Claim Objections

The Examiner objects to claims 2-3 and 12-13 for reciting non-elected sequences and claims 4-5 and 21 for reciting non-elected invention. Applicants respectfully disagree. As indicated by the Examiner in the Restriction Requirement dated May 28, 2009, the restriction requirement between sequences is subject to non-allowance of the generic claims 1 and 2. Additionally, as indicated by the Examiner in the instant Office Action at page 3, the restriction requirement between Groups I-V is also subject to non-allowance of the generic claim 1. Thus, in the event that claims 1 and 2 are found allowable, then rejoinder of the non-elected subject matter that would depend from or otherwise include all the limitations of the allowed claim is respectfully requested. MPEP § 821.04(b). Upon allowance of the generic claims (claims 1 and 2) or the claims directed to the elected species, Applicants respectfully request rejoinder of the non-elected species. 37 CFR § 1.141; MPEP § 809.02(a).

Claim 1 is objected to for informality and claim 2 is objected to as being confusing. In response, claims 1 and 2 have been amended without prejudice or disclaimer by adopting the Examiner's suggestions. Support to the amendments made is found *inter alia* in the original claims. No new matter has been added.

Claims 13 and 17-20 are objected to as being in improper form. In response, the multiple dependency in claim 12, from which claim 13 is dependent, and claim 20 has been removed without prejudice or disclaimer. No new matter has been added by this amendment.

In view of the present amendments, it is believed that the above objections are overcome. Accordingly, reconsideration and withdrawal of the objections is respectfully requested.

Claim Rejections – 35 U.S.C. § 112

Claims 1-23 are rejected for allegedly lacking an enabling disclosure and for allegedly failing to comply with the written description requirement. Applicants respectfully disagree. However, to expedite prosecution, the claims have been amended without prejudice or disclaimer to recite the claimed method with more specificity. Applicants respectfully submit that the claims as amended overcome both rejections for the following reasons.

Enablement Rejection

Claims 1-23 are rejected for alleged lack of an enabling disclosure.

The Examiner alleges that the specification is enabling only for dsRNA comprising SEQ ID NO: 1 or a nucleic acid encoding SEQ ID NO: 2 and its use in generating or increasing at least one pathogen resistance in a plant/plant cell, but not other embodiments including the use of sense, antisense, or dsRNA of variants/homologues/functional equivalents of SEQ ID NO: 1 or a nucleic acid encoding SEQ ID NO: 2, and a transgenic animal comprising a nucleic acid encoding a NAPDH oxidase. The Examiner further asserts that no guidance is provided for a method other than transient transformation of barley cells. Additionally, the Examiner also contends that the specification does not provide guidance for any modifications to SEQ ID NO: 1 and cites to Schiene *et al.* for support of unpredictability in using antisense to inhibit expression of an endogenous protein to induce disease resistance. Applicants respectfully disagree.

It is noted initially that the disclosure provided in the specification is presumptively enabling. The manner of making and using the claimed invention must be taken as in compliance with the first paragraph of 35 U.S.C. §112, unless there is objective evidence or scientifically based reasoning inconsistent with the specification. *See In re Marzocchii and Horton*, 169 U.S.P.Q. 367 (C.C.P.A. 1971). "It is the Patent Office's burden to present evidence that there is some reason to dispute the enablement provided in the specification. Unsupported speculation or conjecture on that the invention 'might not work' will not support a rejection based on 35 U.S.C. §112, first paragraph." *Id.* Simply pointing to the absence of a working example provides neither objective evidence nor reasoning in support of the rejection, and accordingly, a *prima facie* case of non-enablement on this ground has not been made out. Moreover, there has never been a requirement that every species encompassed by a claim must be disclosed or exemplified in a working example. *In re Angstadt*, 537 F.2d 498 (CCPA 1976). Further, a patent need not disclose what is well known to those skilled in the art and preferably omits that which is well known to those skilled and already available to the public. *In re Buchner*, 929 F.2d 660, 661 (Fed. Cir. 1991). Additionally, even though practicing the full scope of the claims might have required some amount of experimentation, if the experimental techniques are well-known in the art, the experimentation is routine and not undue. See *Ex parte*

Kubin, 83 USPQ2d 1410 (B.P.A.I. 2007), *aff'd on other ground*, 90 USPQ 2d 1417 (Fed. Cir. 2009).

Here, as acknowledged by the Examiner, the specification provides working examples using the full-length dsRNA comprising antisense and sense sequences of SEQ ID NO: 1. The working examples provided in the specification describe, in detail, how to clone a cDNA encoding a NAPDH oxidase (Example 2), how to synthesize *in vitro* dsRNA of a NAPDH oxidase (Example 3), how to transiently transform dsRNA into a cell to create RNA interference (Example 4), and how to evaluate the pathogen resistance in the transformed cells (Example 4). In addition to the use of dsRNA, the specification further provides working example in inhibiting NAPDH oxidase using diphenyleneiodonium chloride (Example 5). The methodologies described in the specification are applicable not only to the full-length of SEQ ID NO: 1 as exemplified, but also any other sequences encoding NAPDH oxidases for which the reduction of protein quantity, activity or function is desired. Moreover, it is respectfully submitted that other methodologies such as those based on the use of sense or antisense of a sequence in reducing quantity, activity or function of the encoded protein are within the knowledge of one skilled in the art. Thus, although some testing and screening would be required when different methodology is used and/or different NAPDH oxidase genes or parts thereof are used, such testing and screening would not be extensive and is routine in nature, and thus, not undue. On these facts, an analysis under *In re Wands* supports enablement. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988) (routine screening of hybridomas was not "undue experimentation;" the involved experimentation can be considerable, so long as "routine").

Following the guidance in the specification, taken together with the knowledge of the art, Applicants have produced further experimental data using a different NAPDH oxidase coding sequence with a different method in inhibiting the quantity, activity or function of the encoded NAPDH oxidase to further illustrate the enablement of the specification. For example, knock-out Arabidopsis plants were generated using the sequence of SEQ ID NO: 11, which encodes a NAPDH oxidase from *Arabidopsis thaliana*. As depicted on the attached figure, the knock-out plants exhibit an increased percentage of 0-30% infected area ("robhF," black bar) and decreased percentage of higher infected area (i.e. 30-60% infected area) when compared with the wild-type control plants ("ROBHF," white bar). As would be understood by one of ordinary skill in the

art, such data indicates that the knock-out plants exhibits an increased resistance to the pathogen tested. Thus, through routine experiments and as would be known by one skilled in the art following the description and guidance of the specification, one skilled in the art would know how to make and use the claimed method.

The attached figure can be verified (in a declaration) if necessary.

Additionally, Applicants wish to draw the Examiner's attention to the additional sequences encoding NAPDH oxidases disclosed in the specification, for example, at page 23, line 30, through page 24, line 12. Upon aligning those sequences, one skilled in the art would recognize which amino acid residues are conserved among species and thus, potentially important to the function and activity of the protein and should not be modified. Such conserved regions among different NAPDH oxidases are exemplified in the specification at page 24, lines 14-28.

In view of the detailed description, guidance, working examples, knowledge of the art, and high level of skill, the specification enables the full scope of the claims as amended without undue experimentation. On these facts, an analysis under *In re Wands* supports enablement. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). In this case, any required experimentation would not be extensive and is routine in nature.

As provided herein, Applicants respectfully submit that the art and the specification provide ample guidance and predictability for the present claims as also demonstrated in the attached figure and the Examiner has not presented the evidence necessary to dispute the enablement provided in the instant specification. Because the Patent Office has not met its burden, reconsideration and withdrawal of the enablement rejections is respectfully requested.

Written Description Rejection

Claims 1-23 are further rejected for allegedly failing to comply with the written description requirement.

The Examiner alleges that the nucleic acids employed in the claimed method are described by function only, *i.e.* capable of reducing an amount/activity/function of a NADPH oxidase in a plant. The Examiner further asserts that functional equivalents are not described and that the composition and structure of these nucleic acid sequences are unknown. According to

the Examiner, the specification does not describe a representative number of species capable of reducing an amount/activity/function of a NADPH oxidase in any organism. The Examiner additionally contends that only nucleic acids encoding dsRNA NADPH oxidases from barley comprising SEQ ID NO: 1, transgenic plants, expression cassette/vector comprising said nucleic acids and methods that employ said nucleic acids are described. Applicants respectfully disagree and traverse the rejection.

The "written description" requirement under 35 U.S.C. § 112, first paragraph, serves both to satisfy the inventor's obligation to disclose the technologic knowledge upon which the patent is based, and to demonstrate that the patentee was in possession of the invention that is claimed. *Capon v. Eshhar*, 418 F.3d 1349, 1357, 76 USPQ2d 1078, 1084 (Fed. Cir. 2005); *see also* MPEP § 2163. Possession may be shown in a variety of ways including description of an actual reduction to practice. *See* MPEP § 2163.

The present application describes an actual reduction to practice using constructs comprising SEQ ID NO: 1, for example, in Examples 2-4. Thus, possession of the claimed method is shown, and the rejection should be withdrawn.

It is further noted that, as recited in claim 1, the method according to the present application directs to generate or increase the resistance to at least one pathogen in plants by reducing quantity, activity or function of an NADPH oxidase. Thus, contrary to the Examiner's characterization, the genus recited in the claim that a representative number of species need be shown to demonstrate that the patentee was in possession of such a genus is the genus of NADPH oxidases. As such, Applicants respectfully submit that the specification provides a representative number of NADPH oxidases. In addition to SEQ ID NO: 2 that is encoded by SEQ ID NO: 1, the specification also discloses additional NAPDH oxidases by their actual sequence, i.e. SEQ ID NO: 4, 6, 8, 10, 12, 14, 16, 18, 20, or 22. Moreover, as discussed above, the specification also discloses additional NAPDH oxidases by their GenBank accession number, for example, at page 23, line 30, through page 24, line 12. It is therefore respectfully submitted that the numerous species disclosed in the specification, either by their actual sequence or by their accession number, constitute a representative number of species of the claimed genus as recited in claim 1 under the standard of *Regents v. Lilly*. See *Regents of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997) (holding that a "description

of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs...").

Applicants further submit that the species disclosed in the specification also constitute a representative number of species of the claimed genus as recited in claims 2 and 3. In the amended claim 2, the genus is further defined by the presence of at least one sequence motif selected from a group of 11 different motifs. In the amended claim 3, the genus is further defined by the degree of sequence identity shared with one of the sequences of SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, and 22. As shown in the attached sequence alignment between the disclosed SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, and 22, all of these sequences comprise at least one of the sequence motifs recited in claim 2. The degree of sequence identity shared between these sequences ranges from 47% to 98% as summarized in the attach table. Accordingly, all of these 11 sequences fall within the scope of the genus as recited in claims 2 and 3 as amended and thus clearly constitute a "representative" number of species of the claimed genus. Since a representative number of species is provided in the specification and the Examiner has not provided reasons why it is not, the specification provides adequate written description for the present claims. See *In re Marzocchi*, 439 F.2d 220, 224 (CCPA 1971); MPEP § 2163.04 (written description under 35 U.S.C. § 112, first paragraph, is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption).

For at least the above reasons and in light of the present amendments, it is respectfully submitted that the specification provides adequate written description for the claims as amended. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the above remarks and further in view of the above amendments, Applicants respectfully request withdrawal of the rejections and allowance of the claims. If any outstanding issues remain, the Examiner is invited to telephone the undersigned at the number given below.

As mentioned above, the attached figure can be verified (in a declaration) if necessary.

This response is filed within the three-month period for response from the mailing of the Office Communication. No fee is believed due. However, if a fee is due, please charge our

Deposit Account No. 03-2775, under Order No. 12810-00067-US from which the undersigned is authorized to draw.

Respectfully submitted,

By /s/ Hui-Ju Wu
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Attachments:

1. Figure showing additional experimental data using SEQ ID NO: 11 knock-out plants.
2. Sequence alignment between SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, and 22.
3. Table summarizing the degree of sequence identity between SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, and 22.